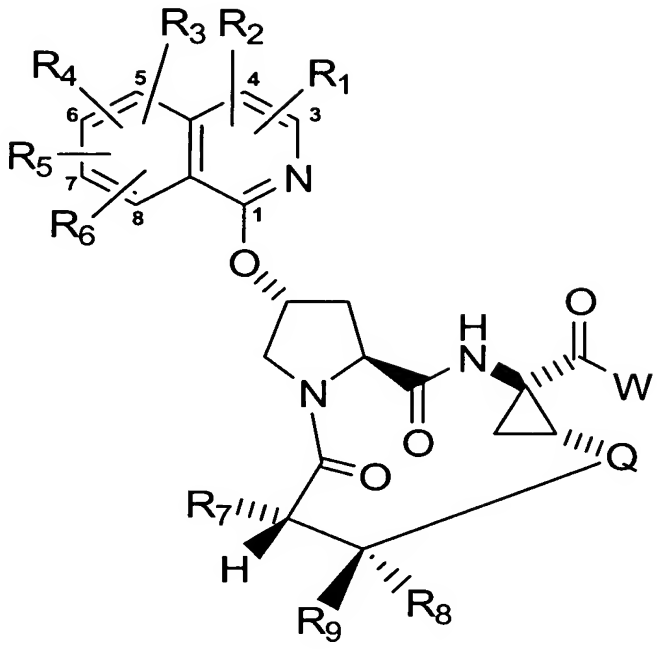
CLAIMS

What is claimed is:

1. A compound of formula I:



I

wherein:

(a) R_1, R_2, R_3, R_4, R_5 and R_6 are each independently H; C_{1-6} alkyl; C_{3-7} cycloalkyl; C_{1-6} alkoxy; C_{3-7} cycloalkoxy; halo-C_{1-6} alkoxy; halo-C_{1-6} alkyl; cyano; halo; hydroxyl; C_{1-6} alkanoyl; nitro; amino; mono or di-(C_{1-6}) alkyl amine; mono or di-(C_{3-7}) cycloalkyl amine; mono or di-C_{1-6} alkylamide; mono or di-(C_{3-7}) cycloalkyl amide; carboxyl; (C_{1-6}) carboxyester; thiol; C_{1-6} thioalkyl ; C_{1-6} alkylsulfoxide;C_{1-6} alkylsulfone; C_{1-6} alkylsulfonamide; C_{6-10} aryl optionally substituted with Het; C_{7-14} alkylaryl; C_{6-10} aryloxy; C_{7-14} alkylaryloxy; 4-7 membered monocyclic heteroaryloxy; or Het; said R_1 to R_6 optionally attached to the isoquinoline group by a C_{1-6} alkyl linking group;

(b) R_7 is NH_2 or $-NR_{10}R_{11}$; wherein R_{10} is C_{1-6} alkyl, C_{1-6} haloalkyl, $C(O)-NR_{12}R_{13}$, $C(O)-OR_{14}$, $C(O)-SR_{15}$, or $-C(O)-R_{16}$; R_{11} is H, C_{1-6} alkyl or C_{1-6} haloalkyl, provided that if either R_{12} or R_{13} is H then R_{11} is H;
R_{12} and R_{13} are each independently H; C_{1-6} alkyl, C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, each optionally substituted with halo, C_{1-3} alkoxy, C_{1-3} haloalkoxy, C_{1-3} alkyl or C_{1-3} haloalkyl; or aryl; and wherein R_{12} and R_{13} together with the nitrogen to which they are bonded can form a 4-7 membered heterocycle;
R_{14} and R_{15} are each independently C_{1-6} alkyl, C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, each optionally substituted with halo, C_{1-3} alkoxy, C_{1-3} haloalkoxy, C_{1-3} alkyl or C_{1-3} haloalkyl; aryl or Het; R_{16} is H; C_{1-6} alkyl, C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, each optionally substituted with halo, C_{1-3} alkoxy, C_{1-3} haloalkoxy, C_{1-3} alkyl or C_{1-3} haloalkyl; aryl or Het;

(c) R_8 and R_9 are each independently H or C_{1-3} alkyl optionally substituted with halo, or C_{1-3} alkoxy, or C_{1-3} haloalkoxy;

(d) Q is a C_{3-9} saturated or unsaturated chain optionally containing one to three heteroatoms independently selected from O, $S(O)_m$; wherein m is 0, 1 or 2, or NR_{17}, wherein R_{17} is H; C_{1-6} alkyl or C_{1-6} cycloalkyl, each optionally substituted with halo, C_{1-6} alkoxy, cyano or C_{1-6} haloalkoxy; $-C(O)-R_{18}$, $C(O)-OR_{19}$, $C(O)-NR_{20}R_{21}$ or $-SO_2R_{22}$; R_{18}, R_{20}, and R_{21} are each independently H; C_{1-6} alkyl or C_{1-6} cycloalkyl, each optionally substituted with halo, C_{1-6} alkoxy, cyano or C_{1-6} haloalkoxy; R_{19} is C_{1-6} alkyl or C_{1-6} cycloalkyl, each optionally substituted with halo, C_{1-6} alkoxy, cyano or C_{1-6} haloalkoxy;
R_{22} is aryl, C_{1-6} alkyl or C_{1-6} cycloalkyl, each optionally substituted with halo, C_{1-6} alkoxy, cyano or C_{1-6} haloalkoxy; and

(e) W is OH, $-NH-SO_n-R_{23}$, or $NH-SO_n-R_{24}$; wherein n is 1 or 2, R_{23} is C_{1-8} alkyl, C_{4-10} alkylcycloalkyl, unsubstituted C_{3-7} cycloalkyl, or cyclopropyl or cyclobutyl optionally substituted with C_{7-9} alkylaryl or C_{1-4} alkyl optionally

substituted with halo, C_{1-3} alkoxy, cyano, amine, mono or di-C_{1-6} alkylamine, mono or di-C_{1-6} alkylamide or carboxylate; and R_{24} is C_{6-10} aryl or Het;

or a pharmaceutically acceptable enantiomer, diastereomer, salt, solvate or prodrug thereof.

2. The compound of Claim 1 wherein R_1 is bonded to the C_3 position and is selected from H; C_{1-6} alkyl; C_{3-7} cycloalkyl; C_{1-6} alkoxy; C_{3-7} cycloalkoxy; halo-C_{1-6} alkoxy; halo-C_{1-6} alkyl; cyano; halo; C_{1-6} alkanoyl; mono or di-(C_{1-6}) alkyl amine; mono or di-C_{1-6} alkylamide; carboxyl; C_{6-10} aryl optionally substituted with Het; C_{7-14} alkylaryl; C_{6-10} aryloxy or Het.

3. The compound of Claim 1 wherein R_2, R_3, and R_4 are bonded to the C_4, C_5 and C_6 positions, respectively, and are each independently selected from H; C_{1-6} alkyl; C_{3-7} cycloalkyl; C_{1-6} alkoxy; C_{3-7} cycloalkoxy; halo-C_{1-6} alkoxy; halo-C_{1-6} alkyl; cyano; halo; hydroxyl; C_{1-6} alkanoyl; mono or di-(C_{1-6}) alkyl amine; mono or di-(C_{3-7}) cycloalkyl amine; mono or di-C_{1-6} alkylamide; mono or di-(C_{3-7}) cycloalkyl amide; carboxyl; C_{6-10} aryl optionally substituted with Het; C_{7-14} alkylaryl; C_{6-10} aryloxy; or Het.

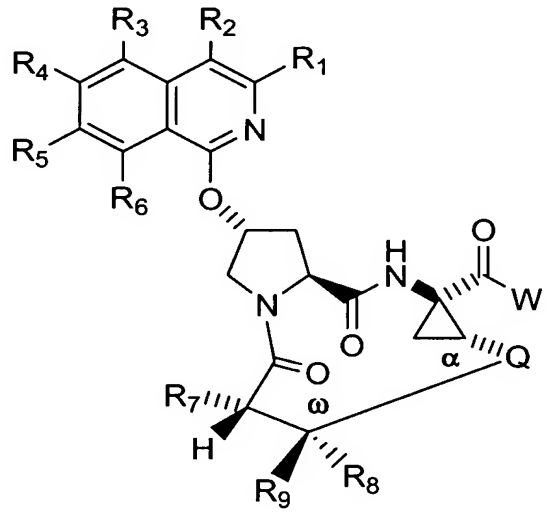
4. The compound of Claim 1 wherein R_5 and R_6 are bonded to the C_7 and C_8 positions, respectively, and are each independently selected from H; C_{1-3} alkyl; C_{3-4} cycloalkyl; C_{1-3} alkoxy; C_{3-4} cycloalkoxy; halo-C_{1-3} alkoxy; halo-C_{1-3} alkyl; cyano; halo; hydroxyl; C_{1-3} alkanoyl; mono or di-(C_{1-3}) alkyl amine; mono or di-(C_{3-4}) cycloalkyl amine; mono or di-C_{1-3} alkylamide; mono or di-(C_{3-4}) cycloalkyl amide; or carboxyl.

5. The compound of Claim 1 wherein Q is a C_{3-9} saturated or unsaturated chain optionally containing one to three heteroatoms independently selected from O, $S(O)_m$; wherein m is 0, 1 or 2, or NR_{17}, wherein R_{17} is H; C_{1-6} alkyl, C_{1-6} cycloalkyl, -C(O)-R_{18}, C(O)-OR_{19}, C(O)-$NR_{20}R_{21}$ or -SO_2R_{22}.

6. The compound of Claim 5 wherein R_{18}, R_{20},and R_{21} are each independently H; C_{1-6} alkyl or C_{1-6} cycloalkyl; R_{19} is C_{1-6} alkyl or C_{1-6} cycloalkyl; and R_{22} is aryl, C_{1-6} alkyl or C_{1-6} cycloalkyl, each optionally substituted with halo.

7. The compound of Claim 1 wherein W is OH, - NH-SO_n-R_{23}, or NH-SO_n- R_{24} wherein n is 1 or 2, R_{23} is unsubstituted C_{3-7} cycloalkyl, or cyclopropyl or cyclobutyl optionally substituted with C_{7-9} alkylaryl or C_{1-4} alkyl; and R_{24} is C_{6-10} aryl or Het.

8. A compound of formula II:



II

wherein:

(a) R_1 is H; C_{1-6} alkyl; C_{3-7} cycloalkyl; C_{1-6} alkoxy; C_{3-7} cycloalkoxy; halo-C_{1-6} alkoxy; halo-C_{1-6} alkyl; cyano; halo; C_{1-6} alkanoyl; mono or di-(C_{1-6}) alkyl amine; mono or di-C_{1-6} alkylamide; carboxyl; C_{6-10} aryl optionally substituted with Het; C_{7-14} alkylaryl; C_{6-10} aryloxy or Het; said R_1 optionally attached to the isoquinoline group by a C_{1-6} alkyl linking group;
R_2, R_3, and R_4 are each independently H; C_{1-6} alkyl; C_{3-7} cycloalkyl; C_{1-6}

alkoxy; C_{3-7} cycloalkoxy; halo-C_{1-6} alkoxy; halo-C_{1-6} alkyl; cyano; halo; hydroxyl; C_{1-6} alkanoyl; mono or di-(C_{1-6}) alkyl amine; mono or di-(C_{3-7}) cycloalkyl amine; mono or di-C_{1-6} alkylamide; mono or di-(C_{3-7}) cycloalkyl amide; carboxyl; C_{6-10} aryl optionally substituted with Het; C_{7-14} alkylaryl; C_{6-10} aryloxy; or Het; said R_2 to R_4 optionally attached to the isoquinoline group by a C_{1-3} alkyl linking group; R_5 and R_6 are each independently H; C_{1-3} alkyl; C_{3-4} cycloalkyl; C_{1-3} alkoxy; C_{3-4} cycloalkoxy; halo-C_{1-3} alkoxy; halo-C_{1-3} alkyl; cyano; halo; hydroxyl; C_{1-3} alkanoyl; mono or di-(C_{1-3}) alkyl amine; mono or di-(C_{3-4}) cycloalkyl amine; mono or di-C_{1-3} alkylamide; mono or di-(C_{3-4}) cycloalkyl amide; or carboxyl;

(b) R_7 is NH_2 or $-NR_{10}R_{11}$; wherein R_{10} is C_{1-6} alkyl, C_{1-6} haloalkyl, $C(O)-NR_{12}R_{13}$, $C(O)-OR_{14}$, or $-C(O)-R_{16}$; R_{11} is H, C_{1-6} alkyl or C_{1-6} haloalkyl, provided that if either R_{12} or R_{13} is H then R_{11} is H; R_{12} and R_{13} are each independently H; C_{1-6} alkyl, C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, each optionally substituted with halo, C_{1-3} alkoxy, C_{1-3} haloalkoxy, C_{1-3} alkyl or C_{1-3} haloalkyl; and wherein R_{12} and R_{13} together with the nitrogen to which they are bonded can form a 4-7 membered heterocycle; R_{14} and R_{15} are each independently C_{1-6} alkyl, C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, each optionally substituted with halo, C_{1-3} alkoxy, C_{1-3} haloalkoxy, C_{1-3} alkyl or C_{1-3} haloalkyl; R_{16} is H; C_{1-6} alkyl, C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, each optionally substituted with halo, C_{1-3} alkoxy, C_{1-3} haloalkoxy, C_{1-3} alkyl or C_{1-3} haloalkyl; aryl or Het;

(c) R_8 and R_9 are each independently H or C_{1-3} alkyl optionally substituted with halo, or C_{1-3} alkoxy, or C_{1-3} haloalkoxy;

(d) Q is a C_{3-9} saturated or unsaturated chain optionally containing one to three heteroatoms independently selected from O, $S(O)_m$; wherein m is 0, 1 or 2, or NR_{17}, wherein R_{17} is H; C_{1-6} alkyl, C_{1-6} cycloalkyl, $-C(O)-R_{18}$, $C(O)-OR_{19}$, $C(O)-NR_{20}R_{21}$ or $-SO_2R_{22}$; R_{18}, R_{20}, and R_{21} are each independently H; C_{1-6} alkyl or C_{1-6} cycloalkyl; R_{19} is C_{1-6} alkyl or C_{1-6} cycloalkyl; R_{22} is aryl, C_{1-6} alkyl or C_{1-6} cycloalkyl, each optionally substituted with halo; and

(e) W is OH, - NH-SO_n-R_{23} or NH-SO_n- R_{24}, wherein n is 1 or 2, R_{23} is unsubstituted C_{3-7} cycloalkyl, or cyclopropyl or cyclobutyl optionally substituted with C_{7-9} alkylaryl or C_{1-4} alkyl; and R_{24} is C_{6-10} aryl or Het;

or a pharmaceutically acceptable enantiomer, diastereomer, salt, solvate or prodrug thereof.

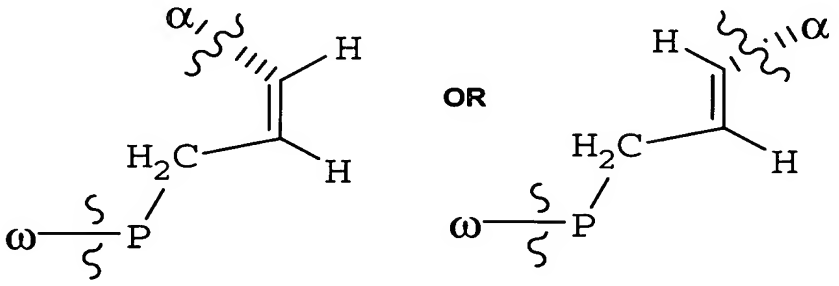
9. The compound of Claim 8 wherein R_1 is H; C_{1-3} alkoxy; mono or di-(C_{1-6}) alkyl amine; a 5 or 6 membered monocyclic heterocycle; or C_{6-10} aryl optionally substituted with a 5 or 6 membered monocyclic heterocycle.

10. The compound of Claim 8 wherein R_2, R_3, R_4 and R_5 are each independently H; C_{1-6} alkoxy; halo-C_{1-6} alkoxy; hydroxyl; or mono or di-(C_{1-6}) alkyl amine.

11. The compound of Claim 8 wherein R_7 is NH_2 or –NHR_{10}; wherein R_{10} is C(O)-N $R_{12}R_{13}$,or C(O)-OR_{14}; and R_{12} and R_{13} are C_{1-6} alkyl optionally substituted with halo; and R_{14} is C_{1-6} alkyl or C_{3-7} cycloalkyl optionally substituted with halo .

12. The compound of Claim 8 wherein Q is a C_{5-7} membered chain having one double bond optionally containing one heteroatom independently selected from O, $S(O)_m$; wherein m is 0, 1 or 2, or NR_{17}, wherein R_{17} is H; C_{1-6} alkyl or C_{1-6} cycloalkyl.

13. The compound of Claim 8 wherein Q has the following structure:

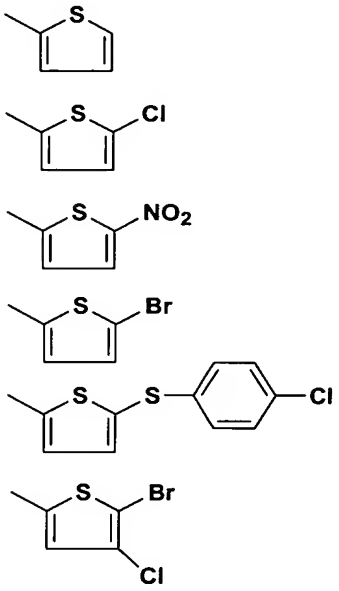


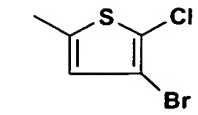
wherein P is a C_3 saturated chain optionally containing one heteroatom independently selected from O, $S(O)_m$; wherein m is 0, 1 or 2, or NR_{17}.

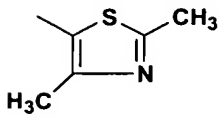
14. The compound of Claim 8 wherein W is - $NH\text{-}SO_n\text{-}R_{23}$, wherein n is 1 or 2 and R_{23} is unsubstituted $C_{3\text{-}7}$ cycloalkyl, or cyclopropyl or cyclobutyl optionally substituted with $C_{7\text{-}9}$ alkylaryl or $C_{1\text{-}4}$ alkyl.

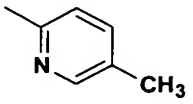
15. The compound of Claim 8 wherein W is $NH\text{-}SO_n\text{-}R_{24}$, wherein n is 1 or 2 and R_{24} is Het.

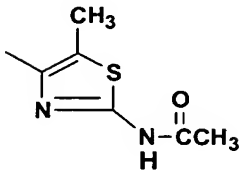
16. The compound of Claim 15 wherein said Het is selected from the group consisting of:

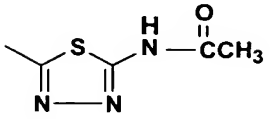


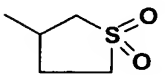


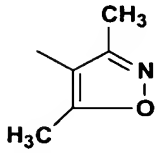


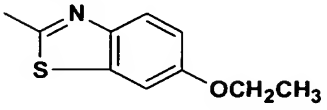


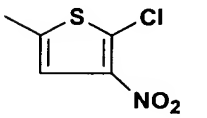




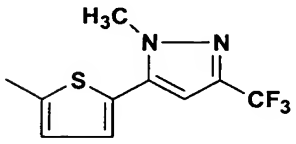




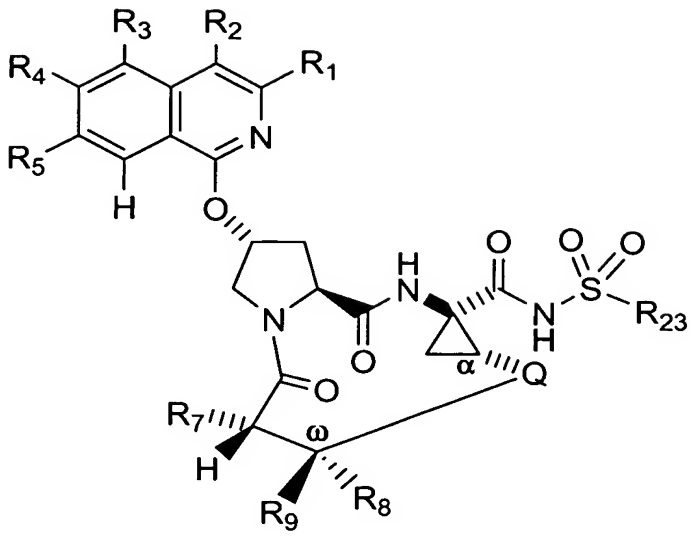




or



5 17. A compound of formula III:



III

wherein:

(a) R_1 is H; C_{1-3} alkoxy; di-(C_{1-6}) alkyl amine; a 5 or 6 membered monocyclic heterocycle; or C_{6-10} aryl optionally substituted with a 5 or 6 membered monocyclic heterocycle; R_2, R_3, R_4 and R_5 are each independently H; C_{1-3} alkoxy; halo; or di-(C_{1-6}) alkyl amine;

(b) R_7 is $-NHR_{10}$; wherein R_{10} is C(O)-NHR_{13},or C(O)-OR_{14}; R_{13} and R_{14} are C_{1-6} alkyl;

(c) Q is a C_{5-7} membered chain having one double bond optionally containing one heteroatom independently selected from O, $S(O)_m$; wherein m is 0, 1 or 2, or NR_{17}, wherein R_{17} is H; C_{1-6} alkyl or C_{1-6} cycloalkyl; and

(d) R_{23} is unsubstituted C_{3-7} cycloalkyl, or cyclopropyl or cyclobutyl optionally substituted with C_{7-9} alkylaryl or C_{1-4} alkyl;

or a pharmaceutically acceptable enantiomer, diastereomer, salt, solvate or prodrug thereof.

18. The compound of Claim 17 wherein R_1 is selected from the group consisting of pyridine, morpholine, piperazine, oxazole, isoxazole, thiazole, imidazole, pyrrole and pyrazole.

19. The compound of Claim 17 wherein R_1 is phenyl optionally substituted with one or more members selected from the group consisting of selected from the group consisting of C_{1-3} alkoxy, halo, carboxyl, di-(C_{1-3}) alkyl amine, C_{1-3} haloalkyl, trifluoromethyl, trifluoromethoxy and hydroxy.

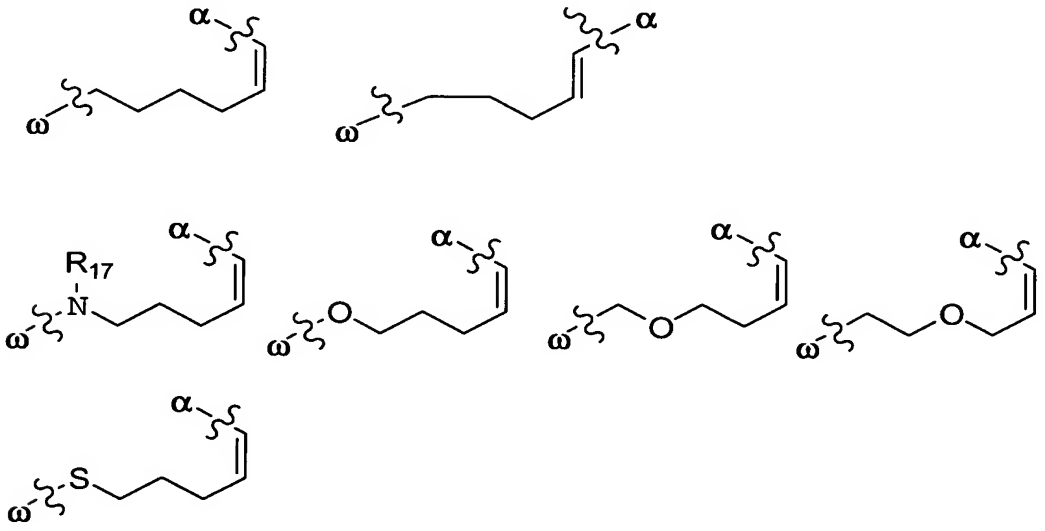
20. The compound of Claim 17 wherein R_1 is di-(C_{1-3}) alkyl amine.

21. The compound of Claim 17 wherein R_1 is piperazine substituted with one or more members selected from the group consisting of C_{1-3} alkyl, C_{5-7} cycloalkyl or pyridine.

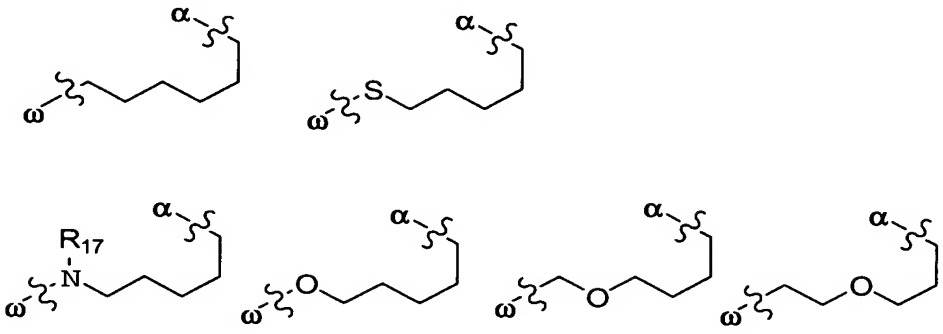
22. The compound of Claim 17 wherein R_2 is chloro or fluoro.

23. The compound of Claim 17 wherein R_2 is di-(C_{1-3}) alkyl amine or methoxy.

24. The compound of Claim 17 wherein Q has a structure selected from the following:



25. The compound of Claim 17 wherein Q has a structure selected from the following:



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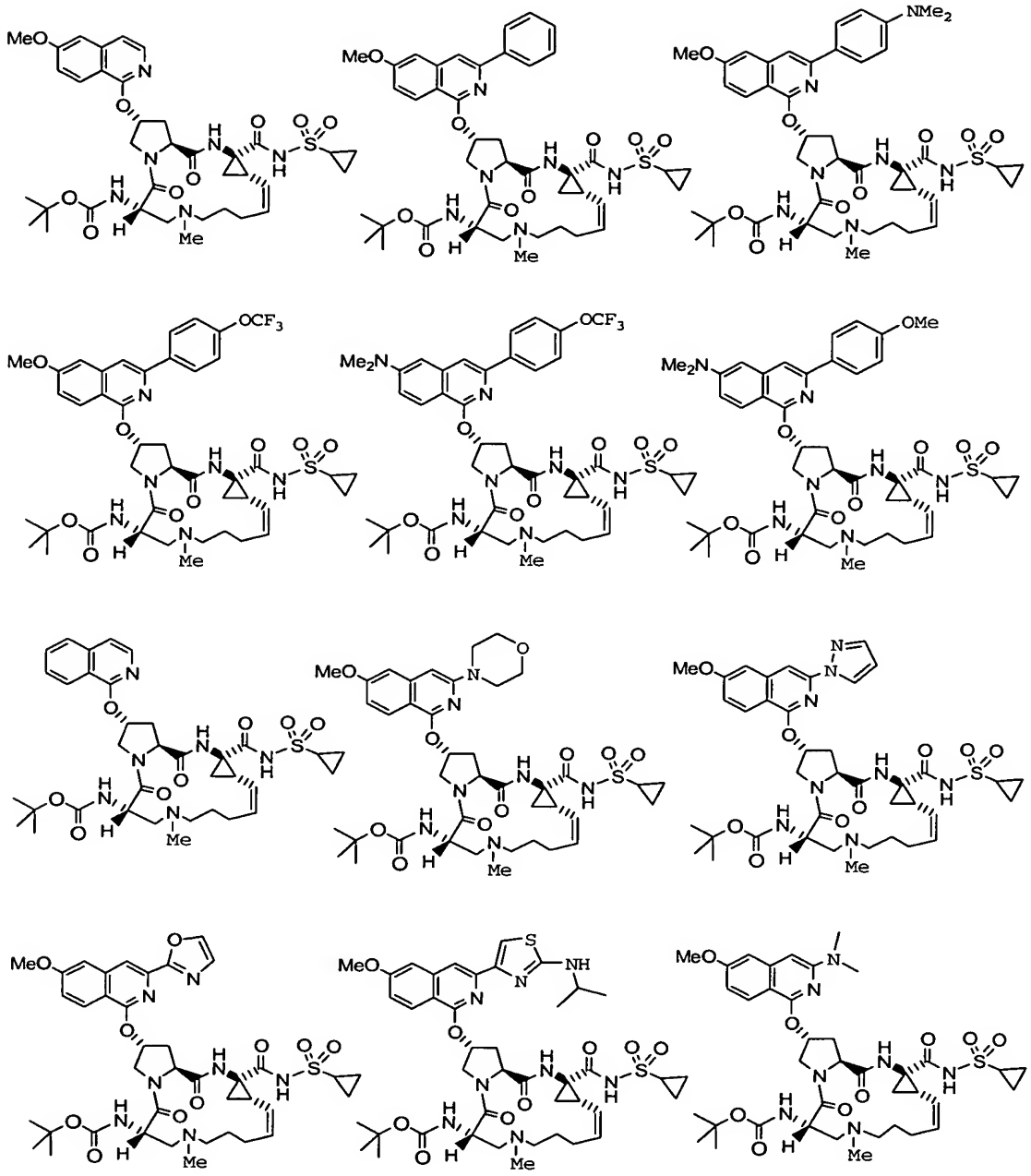
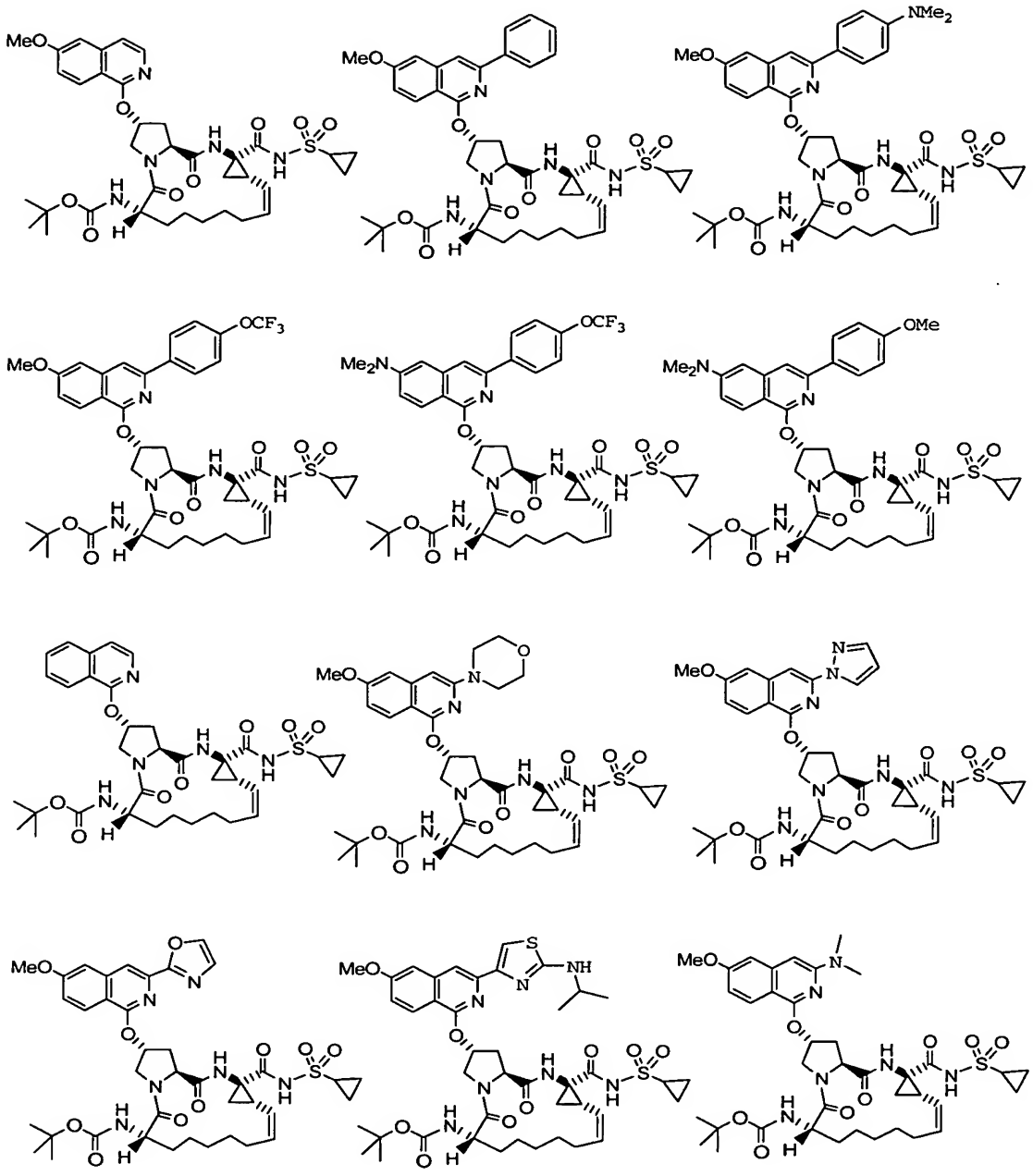
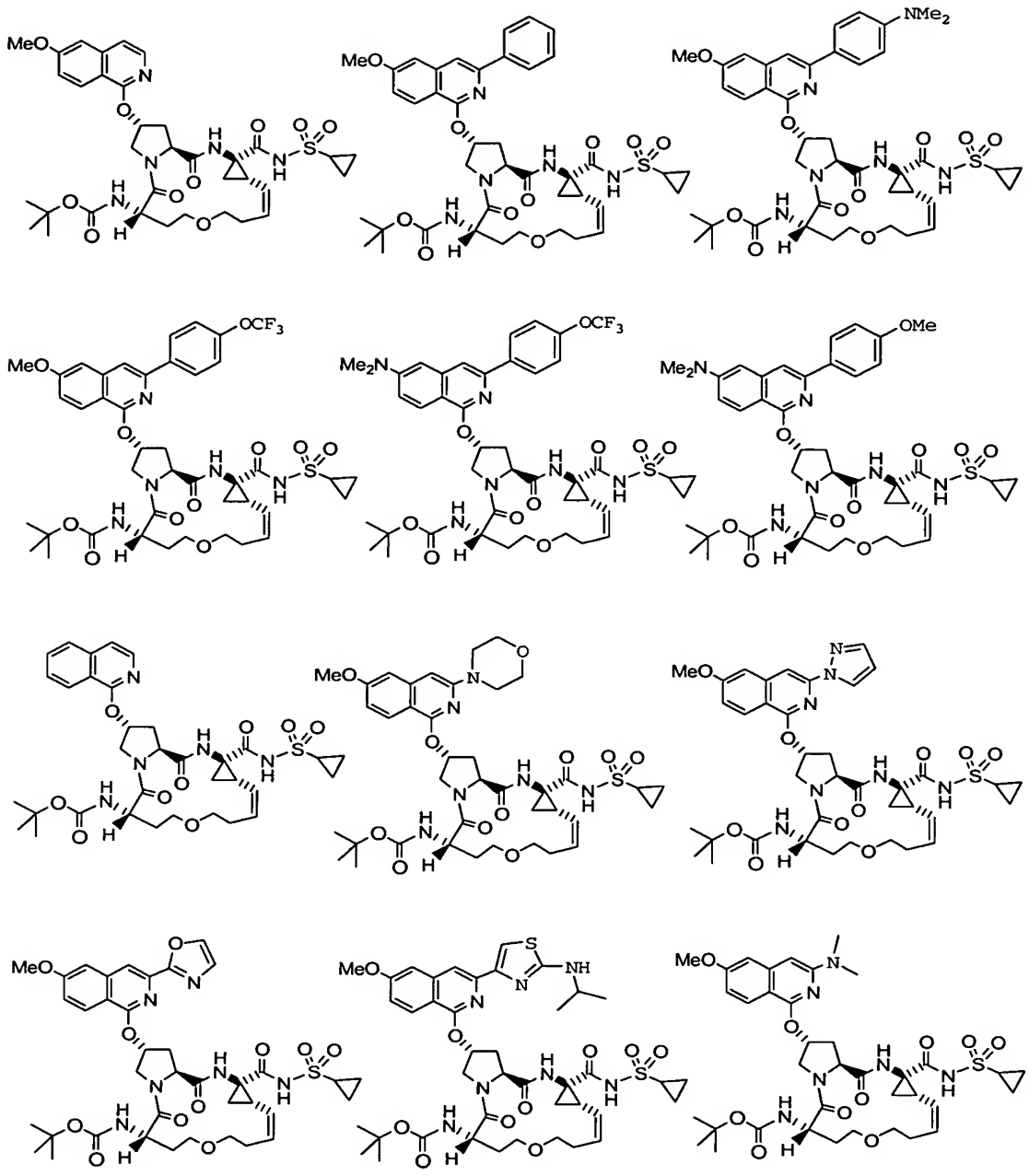
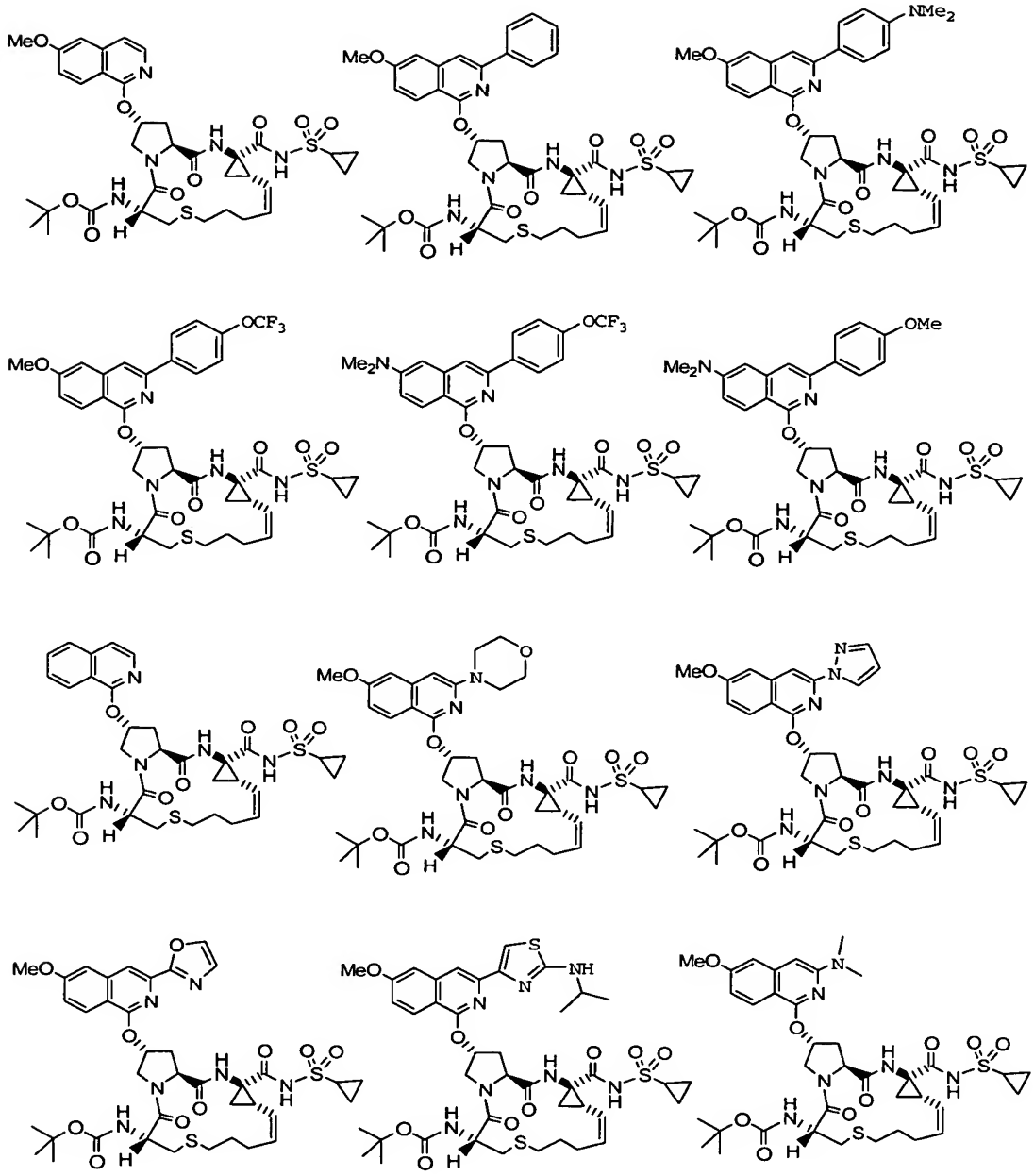
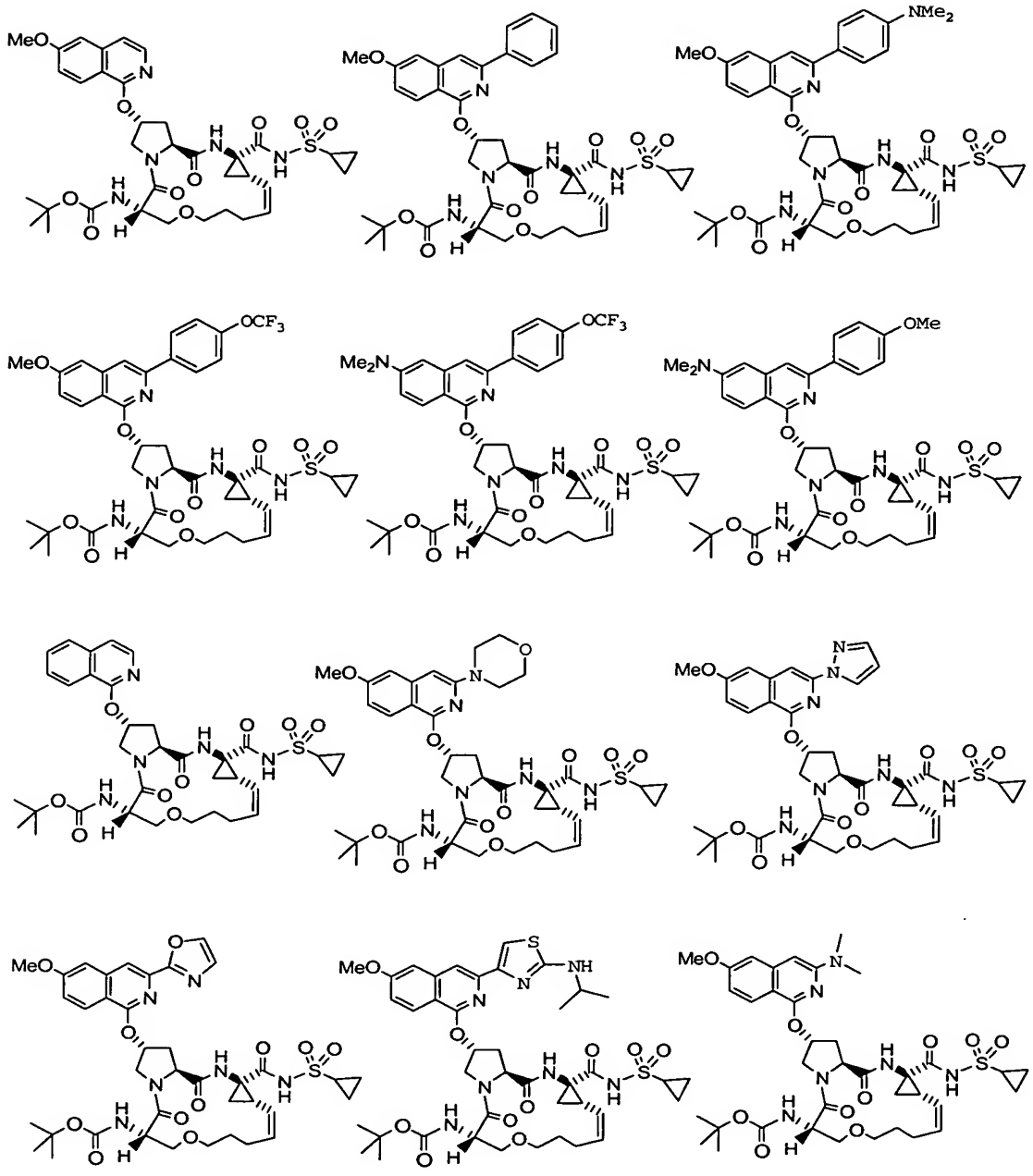
26. A compound selected from the group consisting of

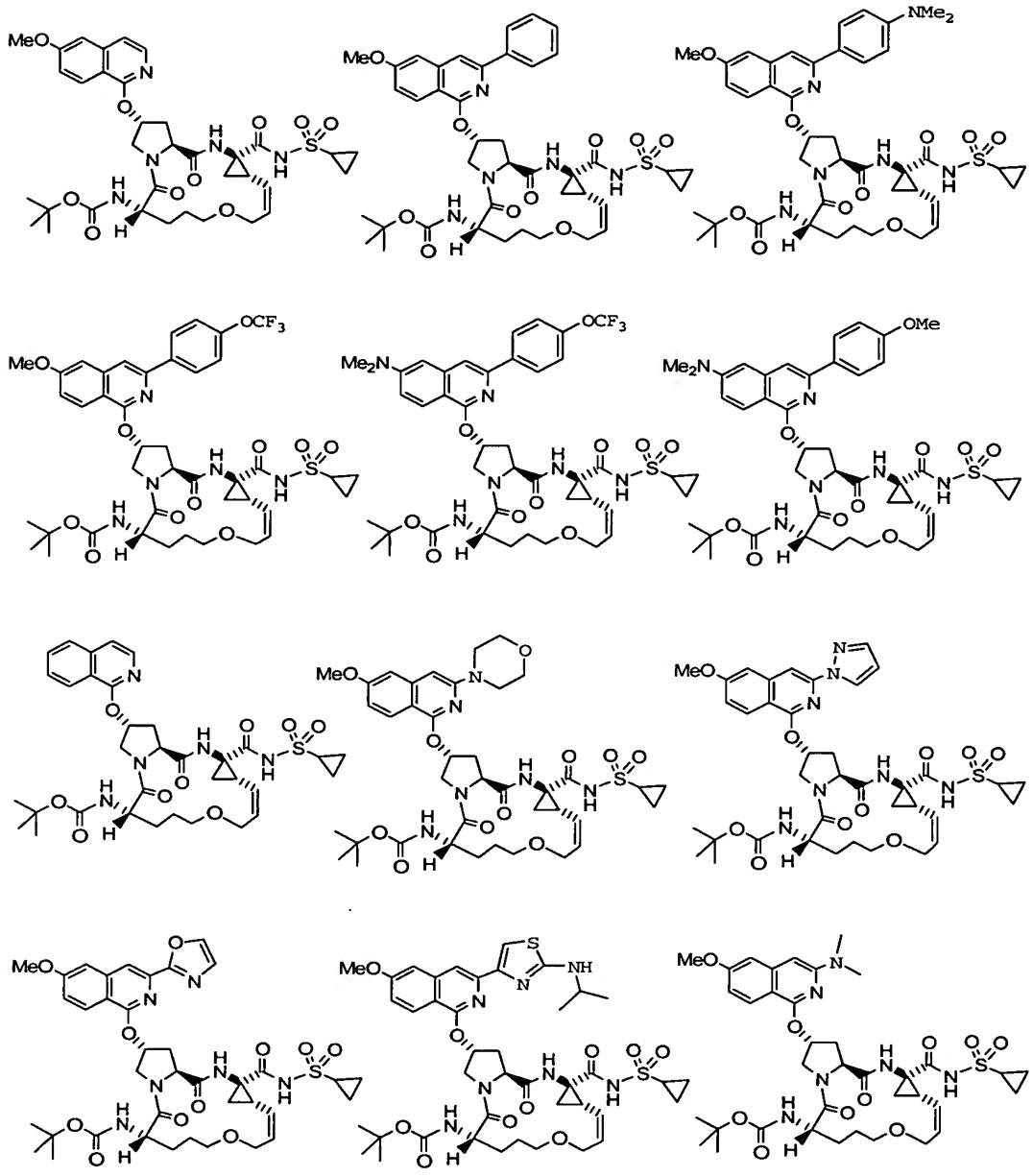












27. A composition comprising the compound of Claim 1 and a pharmaceutically acceptable carrier.

28. The composition according to Claim 27 further comprising a compound having anti-HCV activity.

29. The composition according to Claim 28 wherein the compound having anti-HCV activity is an interferon.

30. The composition according to Claim 29 wherein the interferon is selected from the group consisting of interferon alpha 2B, pegylated interferon alpha, consensus interferon, interferon alpha 2A, and lymphoblastiod interferon tau.

31. The composition according to Claim 28 wherein the compound having anti-HCV activity is selected from the group consisting of interleukin 2, interleukin 6, interleukin 12, a compound that enhances the development of a type 1 helper T cell response, interfering RNA, anti-sense RNA, Imiqimod, ribavirin, an inosine 5'-monophospate dehydrogenase inhibitor, amantadine, and rimantadine.

32. The composition according to the Claim 28 further comprising an interferon and ribavirin.

33. The composition according to Claim 28 wherein the compound having anti-HCV activity is a small molecule compound.

34. The composition according to Claim 28 wherein the compound having anti-HCV activity is effective to inhibit the function of a target selected from the group consisting of HCV metalloprotease, HCV serine protease, HCV polymerase, HCV helicase, HCV NS4B protein, HCV entry, HCV assembly, HCV egress, HCV NS5A protein, IMPDH and a nucleoside analog for the treatment of an HCV infection.

35. A method of inhibiting the function of the HCV serine protease comprising contacting the HCV serine protease with the compound of Claim 1.

36. A method of treating an HCV infection in a patient, comprising administering to the patient a therapeutically effective amount of the compound of Claim 1, or a pharmaceutically acceptable enantiomer, diastereomer, solvate, prodrug or salt thereof.

37. The method according to Claim 36 wherein the compound is effective to inhibit the function of the HCV serine protease.

38. The method according to Claim 36 further comprising administering another compound having anti-HCV activity prior to, after or simultaneously with the compound of Claim 1.

39. The method according to Claim 38 wherein the other compound having anti-HCV activity is an interferon.

40. The method according to Claim 39 wherein the interferon is selected from the group consisting of interferon alpha 2B, pegylated interferon alpha, consensus interferon, interferon alpha 2A, lymphoblastiod interferon tau.

41. The method according to Claim 38 wherein the other compound having anti-HCV activity is selected from the group consisting of interleukin 2, interleukin 6, interleukin 12, a compound that enhances the development of a type 1 helper T cell response, interfering RNA, anti-sense RNA, Imiqimod, ribavirin, an inosine 5'-monophospate dehydrogenase inhibitor, amantadine, and rimantadine.

42. The method according to Claim 38 wherein the compound having anti-HCV activity is a small molecule.

43. The method according to Claim 42 wherein the compound having anti-HCV activity is effective to inhibit the function of a target selected from the group consisting of HCV metalloprotease, HCV serine protease, HCV polymerase, HCV helicase, HCV NS4B protein, HCV entry, HCV assembly, HCV egress, HCV NS5A protein, IMPDH and a nucleoside analog for the treatment of an HCV infection.

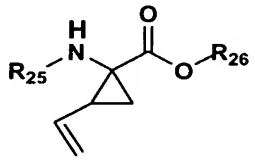
44. The method according to Claim 38 wherein the other compound having anti-HCV activity is effective to inhibit the function of target in the HCV life cycle other than the HCV serine protease.

45. Use of the compound of Claim 1 for the manufacture of a medicament for treating HCV infection in a patient.

46. Use of the composition of Claim 27 for the manufacture of a medicament for treating HCV infection in a patient.

47. A process for resolving a mixture of alkyl ester enantiomers comprising contacting the mixture with an enzyme effective to preferentially promote the hydrolysis of one of the enantiomers; characterized in that the contacting is conducted in the presence of a buffer.

48. The process of claim 47 wherein the alkyl ester has the following formula:



(VIII)

wherein:

R_{25} is an amino protecting group; and
R_{26} is selected from the group consisting of C_{1-10} alkyl, C_{6-14} aryl, C_{7-16} alkylaryl, C_{3-7} cycloalkyl or C_{3-10} alkyl cycloalkyl.

49. The process of claim 47 wherein the buffer is selected from the group consisting of phosphates, borates and carbonates.

50. The process of claim 47 wherein the enzyme is a protease.

51. The process of claim 47 wherein the enzyme is selected from the group consisting of Bacillus globigii, Bacillus licheniformis, Bacillus halodurans, Bacillus clausii , Aspergillus oryzase and mixtures thereof.

52. The process of claim 51 wherein the enzyme is selected from the group consisting of Alcalase® (subtilisin protease), Savinase® (subtilisin protease),

Esperase® (subtilisn protease), Flavourzyme™ (fungal protease) and mixtures thereof.

53. The process of claim 47 wherein the contacting is conducted at pH of from about 7.0 to 11.

54. The process of claim 47 wherein the contacting is conducted at a temperature of from about 30 to 60°C.

55. The process of claim 47 wherein the contacting is conducted for a time of less than about seven days.

56. The process of claim 55 wherein the contacting is conducted for a time of from about two hours to three days.